Protection of Human Subjects

IRB Tutorial

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NPS IRB Chair

Overview

- Background and purpose
- Outline how the process works
- Enumerate what the Institutional Review Board (IRB) and Authorizing Official (AO) look for as criteria for approval
- Discuss case studies to illustrate what this means to your research
- Answer questions

Historical Background

Nuremberg Code/ Declaration of Helsinki

- W.W.II trials for war criminals focused on atrocities committed by Nazi physicians
- Rules established that required informed, voluntary consent
- The Nuremberg Code became the first international standard for the conduct of research
- It was followed by the Declaration of Helsinki in 1964 which further defined ethical principles

Federal Guidelines

- In 1973 DHEW published first regulations to protect human subjects, including establishing IRBs

- National Research Act of 1974 identified 3 ethical principles
  - Respect for persons, beneficence, and justice

- Belmont Report 1979
  - These principles must be included in research sponsored by government

The Belmont Report

Three Basic Principles:

1. Respect for Persons

The principle of respect for persons is captured in the consent process. Freedom to participate and withdraw

2. Beneficence

The principle of beneficence is captured in risk/benefit assessments. Do no harm, maximize benefits, minimize risks

3. Justice

The principle of justice is captured in the fair and diverse selection of research subjects on an individual and social basis

Recent Developments

- Recent developments have brought protection of human subjects issues into public focus
  - Government apology to survivors of Tuskegee syphilis study
  - Gulf war vaccine distribution
  - Research incidents at several major institutions
    - University of Penn
    - Virginia Commonwealth University
  - Increased Congressional/Federal scrutiny
    - New mandates for Protection of Human Subjects training

What Happened at U. Penn.

- Gene transfer study at U. Penn.
  - Use of approved consent procedures
  - Importance of reporting adverse events
  - Conflict of interest
- Research subject died as a result of a gene transfer experiment
- Consent form used to enroll subject was not approved by the IRB; omitted important safety information
- Prior adverse events from this and other gene transfer studies not reported promptly

What Happened at V.C.U.

- Twin study sent questionnaire to subject; opened by subject's father
- Questionnaire asked subject to provide health and behavioral information about parents
- Father filed complaint that he was a subject who had not consented to be in the study
  - IRB and institution not responsive
- Dec 2000: Office of Protection from Research Risks (OPRR) cited lack of gaining informed consent from family members as one reason for restricting human subjects protocols at VCU

Federal Regulations: The Common Rule

Mechanisms for the protection of human subjects in research is established by the Code of Federal Regulations 32 CFR 219 ("The Common Rule")

Adopted by 17 Federal Agencies

Regulations require:

1. Review of research by an Institutional Review Board (IRB)

2. Informed consent of subjects

3. Institutional assurances of compliance

Human Subject

"A living individual about whom an investigator… conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information"

Source: 32 CFR 219.102(f)

Research

"A systematic investigation designed to develop or contribute to generalizable knowledge"

Source: 32 CFR 219.102 (d)

"I'm not trying to sell you anything, sir. I'm doing market research, and all I ask is two or three hours of your time to answer a few thousand questions."

Federal Regulations: The Bottom Line

- **All research involving human subjects**
- **Conducted or supported by a Federal department or agency**
- **Must be reviewed and approved by an Institutional Review Board before Federal funds may be expended, unless determined to be exempt**

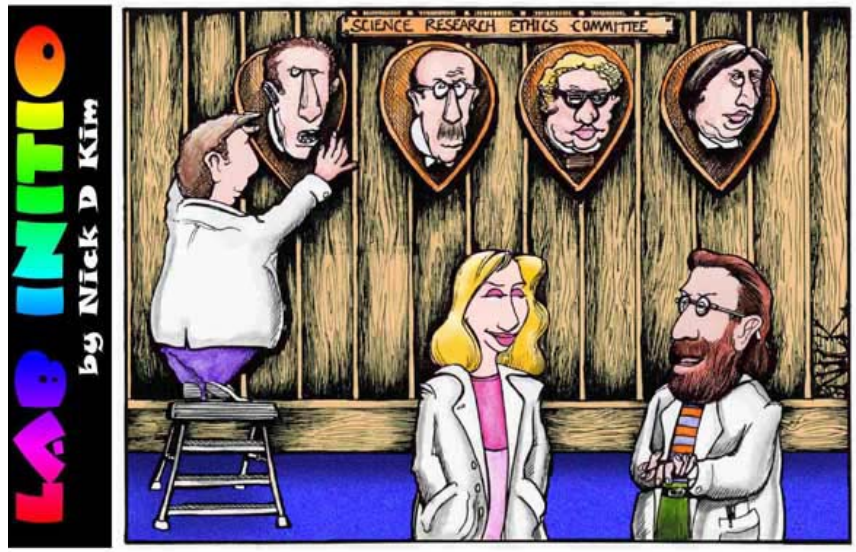
Institutional Review Boards (IRBs)

"A group of at least five individuals with varying backgrounds to promote complete and adequate review of research studies. An IRB conducts the initial & annual reviews of a research study"

Source: 32 CFR 219.107

IRBs

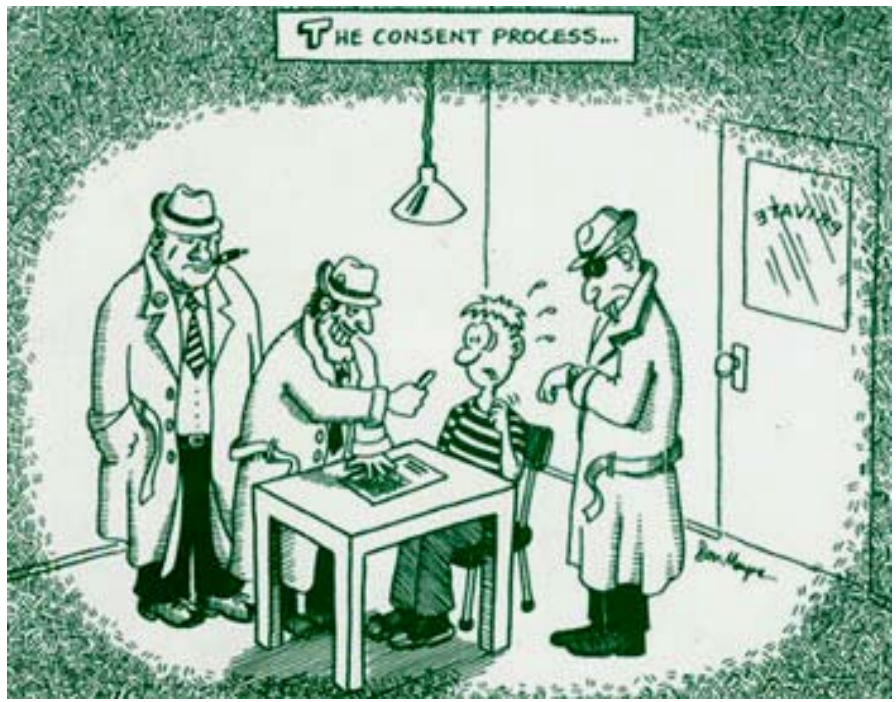
- Review research protocols
- Protect subjects from undue risk and loss of personal rights and dignity
- Approve, require modifications, or disapprove research



"There now...WE get our wish of continuing our work unimpeded, and THEY get their wish of being in a position of direct oversight at all times..."

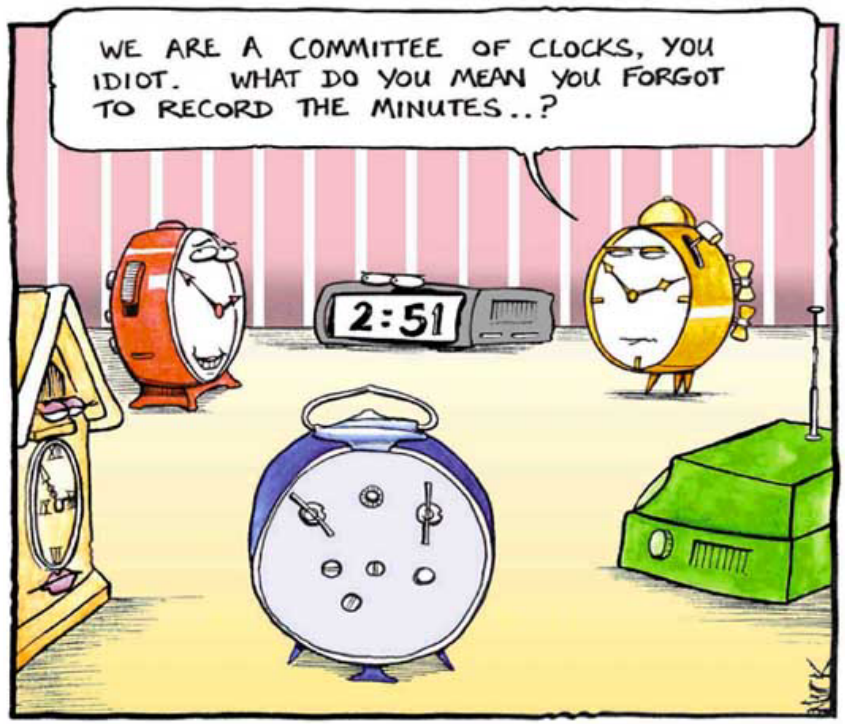
What factors do IRBs consider?

- Nature and extent of potential risk
- Expected benefit of participation to the subject
- How the data will be safeguarded and used
- How subjects will be selected and informed of their rights
- If and how subjects will be identified
- How subjects' consent will be obtained, if required



IRB Records: "Document, Document, Document"

- Research protocols
- Correspondence
- Continuing review documents
- Meeting minutes
- Membership roster
- Written procedures
- Consent forms
- Significant new findings provided to subjects
- Retain for 3 years after study over
- Records available for audit



IRBs: Conflict of Interest

- An IRB may not have members voting on protocols in which she/he has conflicting interest

- A member with a conflict of interest may provide information to the IRB

Conflicting interest:

- "…any interest in the research such that member might be unable to objectively review protocol"

Other Regulations/Requirements

- DOD policy (under revision)
- DON policy
- BUMED policy (under revision)
- NPS policy
- **Bottom line...**

All research involving human beings as participants at NPS must have IRB approval!

NPS IRB – Who's who

- **Jeff Crowson, Ph.D., Acting Chair**
  - **Asst. Professor Rudy Darken, Ph.D., Vice-Chair**
  - **CAPT Nick Davenport, MC, USN - NPS Command Physician**
  - **LCDR Keith Celebrezze, USN - NPS JAG**
  - **LCDR Russ Shilling, MSC, USN, Ph.D. (Past IRB Chair)**
  - **Research Associate Prof. Susan Hutchins**
  - **Senior Lecturer Alice Crawford**
  - **LCDR Mark Smith, USN - Chaplin**
  - **Elaine Shilling, Ph.D. - Ethics Coordinator**

The NPS Approving Official (AO) is delegated to the *Dean of Research* (Dean Leonard Ferrari)

The IRB Administrator is the *Director of Research Administration* (Danielle Kuska)

Overview of the process

- **BUMED reviews policies and procedures and delegates authority to NPS to review and approve research**

- **For each research project, PIs provide input and request approval to proceed**

- **IRB Chair screens submissions and decides on status: exempt, expedited, full review**

Overview of the process

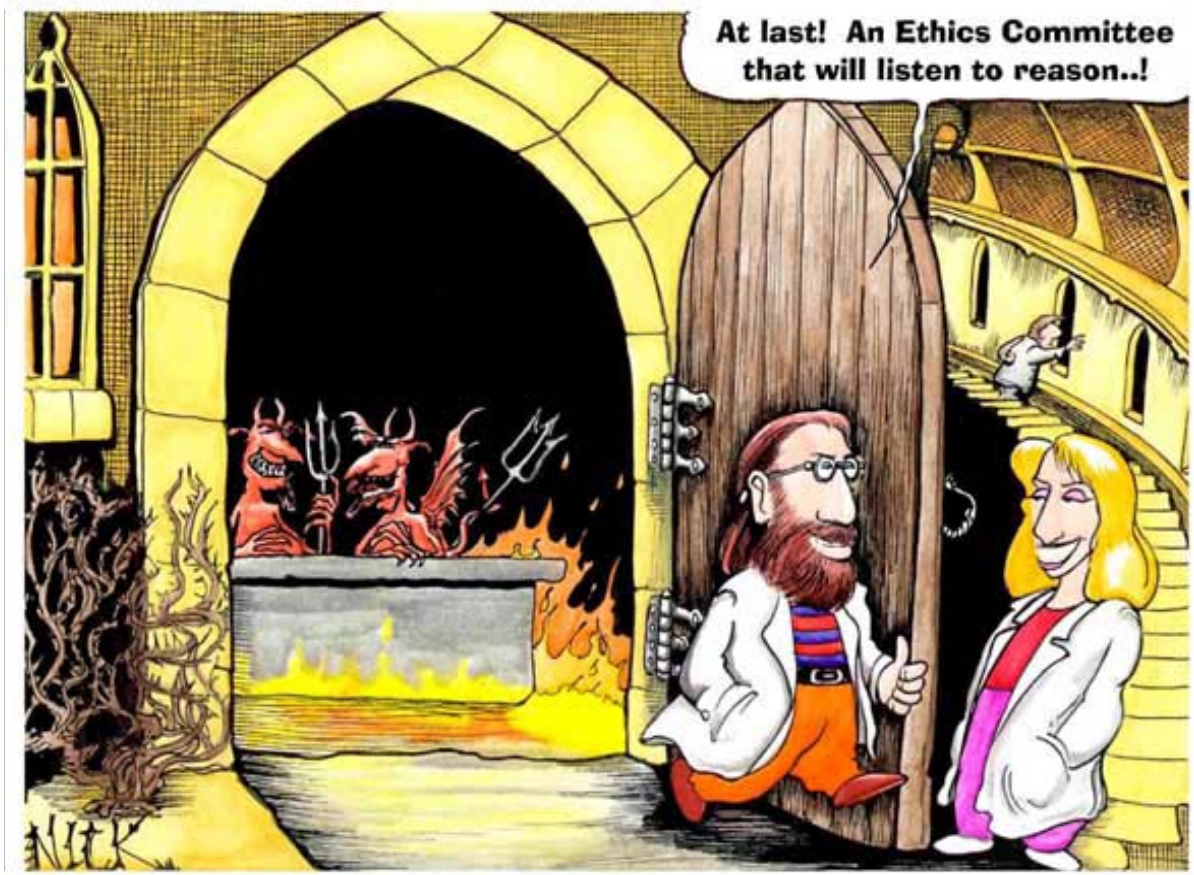
- IRB considers “full review” submissions and makes determinations as required by the regulation; provides oversight and review of “exempt” and “expedited” decisions
- Authorizing Official (AO) confirms actions or requests reconsideration

BUMED Provides Higher level Review

- Copies of submissions and records of IRB/IO actions must be submitted to BUMED
- BUMED may review our actions and override some IRB/AO decisions
- BUMED will conduct periodic site visits to review our policy, procedures, and recordkeeping
- BUMED may withdraw our authority at any time it determines we are in violation of the regulation or DOD, DON, or BUMED policy

Actions the AO can take

- Concur with exemption, approval, or disapproval of a protocol
- Require review of a protocol that was exempted
- Disapprove a protocol that was approved
- Request reconsideration of a protocol that was disapproved
- Authorize release of funds to begin or continue research
- Cannot approve a protocol that was disapproved by the IRB


At last! An Ethics Committee that will listen to reason..!

Role of NPS IRB

- **In carrying out responsibility to protect human subjects, NPS IRB:**
  - **Reviews protocols referred to the Board by Chair**
  - **Reviews all decisions made by Chair**
  - **Provides guidance to Chair and PIs for issues related to**
    - **Informed consent**
    - **Protection of subjects' rights, etc.**


HOW THE IRB MEMBERS SEE THEMSELVES:
45 CFR 46

Role of NPS IRB Chair

- Determine the research is exempt from IRB review
  - Requires short summary of research from PI
- Determine the research qualifies for expedited review
  - Requires full protocol from PI
  - Chair may consult with IRB member in expedited review
- Determine the research requires full board review (e.g., data gathering not anonymous, some potential for harm if released)
  - Requires full protocol from PI and full board review

Exempt Research

Determined by Chair/Reviewed by IRB

Examples of research that is in the exempt category:

1. **Research conducted in educational settings on the effectiveness of or the comparison among instructional techniques, curricula. etc., for program development.**
2. **Use of educational tests, or surveys when the information is collected in such a way that the human subjects cannot be identified and no risk is placed on same.**

Exempt Research

3. **Use of educational tests, or surveys not exempt under #2 may be exempt if subjects are elected or appointed officials or if information collected is absolutely confidential by Federal Statute.**

4. **Study of existing data/records if publicly available & subject can't be identified.**

Exempt Research: Exceptions

- Human subject can be identified and disclosure could place subject at risk
- Pregnant women
- Fetuses
- Human in vitro fertilization
- Prisoners
- "Special" Populations (Military Enlisted Personnel)
- Minors (except educational studies and secondary analysis)

Decisions that Chair /IRB can make

- Recommend approval of research protocol to AO
  - Final concurrence by AO
- Return the protocol to the PI for additional information
- Return the protocol to the PI with a request for specific modifications to the research approach or instrument
- Approve but place restrictions on the research protocol
- Disapprove the research protocol (full IRB only)

Appeal of IRB Actions

- If NPS researcher disagrees with an IRB or Chair decision, he/she may appeal to the Board
- No mechanism for appeal to another committee or IRB
- AO may override the IRB and disapprove a protocol but no authority may override the IRB decision and approve a protocol that was disapproved by the IRB

Subsequent reviews

- PIs must report any changes in protocol for exempted or approved research to Chair for re-review and reconfirmation of exemption or approval status
  - Chair reports changes and decisions to IRB
- IRB must re-review ongoing exempted or approved research at least annually to ensure continued exemption or approval
- PIs must report when research is completed (submit form) so that the IRB can close its files and cease annual reviews

What research is affected and how?

- All research projects require some kind of IRB "sign off"
- Research that does not use human subjects will be signed off as exempt from the regulation
- Some research involving human subjects may be signed off as exempt from review (e.g., tests, anonymous surveys, etc.)
  - Determination made by Chair
  - Subject to review by IRB
- Bottom line: Any research may be reviewed by the IRB

PI Responsibility

- **Investigator must notify Chair/IRB of:**
  - **Proposed changes**
  - **Adverse events**
  - **Complaints**
  - **Protocol violations**
  - **Significant new findings**

Case Study 1

- Conducting survey of attitudes/behaviors
- Survey asks for demographic information (rank, race/ethnic, gender) but no SSN or name
  - Survey asks such questions as:
    - What is your quality of life?
    - What do you think about the base MWR programs?
    - How often do you use the gym/fitness center?
    - How satisfied are you with the Exchange?

Case Study 2

- Conducting research on promotion history of enlisted personnel with certain skills
  - Will extract data from the EMF for all enlisted personnel with certain NECs, of certain paygrades, with certain minimal evaluation marks
  - Will track their job assignments and promotion history over time

Case Study 3

- Subjects participate in economics laboratory experiment
- Subjects are paid based on performance
  - Some individual trials, some in “teams”
  - All subjects receive a “minimum” payment
  - Subjects only paid for performance IF the entire experiment is completed (all sessions)
- Subjects are informed of the process in advance
- SSNs not collected, but sometimes names are obtained

Okay – So what do I do to get approval?

- All NPS IRB Information is located on-line:
- Examples of forms, instructions, etc.

http://www.movesinstitute.org/darken/irb/

1.COMPLETE IRB REQUEST PACKAGE: This includes all documentation you will need to apply for a review of your experiment for approval. This includes the APPLICATION FOR HUMAN SUBJECT REVIEW, A SAMPLE COVER LETTER, CONSENT FORM, MINIMAL RISK CONSENT STATEMENT, and PRIVACY ACT STATEMENT. This is a sample package with all the necessary documents included. You will need to insert the information for your experiment here. Send via e-mail to the IRB Chair.

The End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